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REPLY: The complex miRNAs-p53 signaling network in cardiovascular disease.

We appreciate the comments of Dr. Patanè on our review on microRNAs (miRNAs) in cardiovascular disease. In order to concisely summarise the current knowledge and give our opinion on the way ahead, we have selected key publications that illustrate the great potential of this type of non-coding RNA. The vast number of studies that have been published in the past decade in this field require a balance between addressing the full breadth of cardiovascular disease, and a thorough critical appraisal of these fields.

With this in mind, we briefly touch on miRNA effects on cardiomyocyte apoptosis and regeneration. We highlight the study by Boon et al, reporting a regulatory function of miR-34a on cardiomyocyte survival (1). These results build upon previous studies with an oncological focus, reporting this miRNA to be induced by p53 and acting as a pro-apoptotic signal (2). On the other hand, miRNAs such as miR-590 and -199a were shown to promote cardiomyocyte proliferation through cell cycle re-entry (3). The latter has however also been shown to reduce p53-mediated apoptosis in hypoxic cardiomyocytes (4). These studies illustrate the role that miRNAs seemingly play in apoptosis and proliferation, including the p53 pathway.

Steering cardiomyocytes towards regeneration can certainly be seen as a Holy Grail for heart failure therapy, and we applaud all efforts to further elucidate the mechanisms that are at play. However, in our review we aim to emphasise the systemic effects of miRNAs that come as a natural consequence of their expression across tissues and cell types. This is just as true for p53-related actions of miRNAs as any others, on one hand protecting against dysplasia, and on the other hand restricting repair of dysfunctional tissue in the failing heart. The lack of

techniques that selectively target miRNAs in the heart remains a major impediment to clinical utility. Therefore, we argue for comprehensive evaluation of miRNA effects that takes into account their ubiquitous expression.

REFERENCES

1. Boon RA, Iekushi K, Lechner S, et al. MicroRNA-34a regulates cardiac ageing and function. *Nature* 2013;495:107–10.
2. He L, He X, Lim LP, et al. A microRNA component of the p53 tumour suppressor network. *Nature* 2007;447:1130-1134.
3. Eulalio A, Mano M, Dal Ferro M, et al. Functional screening identifies miRNAs inducing cardiac regeneration. *Nature* 2012;492:376–81.
4. Rane S, He M, Sayed D, et al. Downregulation of miR-199a derepresses hypoxia-inducible factor-1alpha and Sirtuin 1 and recapitulates hypoxia preconditioning in cardiac myocytes. *Circ Res* 2009;104:879-86.